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# Beliefs about medicines and adherence in women with breast cancer on adjuvant endocrine therapy

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## Abstract

The Beliefs about Medicines Questionnaire (BMQ) and Adherence Starts with Knowledge (ASK-12) questionnaire were originally developed and validated in Western populations to assess beliefs and barriers to medication adherence. The study aim is to validate the BMQ and ASK-12 questionnaire for use in a Singapore population with early stage breast cancer. English-speaking women on adjuvant endocrine therapy ($n = 157$) were recruited. The BMQ-Specific showed good internal consistency with structural validity. The internal consistency of BMQ-General and ASK-12 Behaviour scale improved with the new factor structure obtained from exploratory factor analysis. Further studies are needed to confirm these factor structures.

## Keywords

adjuvant endocrine therapy, breast cancer, medication adherence, validation

## Background

In Singapore, breast cancer accounts for 29.1% of all cancers diagnosed in women (National Registry of Diseases Office, 2015). It is also the leading cause of cancer mortality among women. According to a regional hospital-based registry of breast cancer patients in Singapore and Malaysia (Pathy et al., 2011), 66% of patients with known histopathological results are either estrogen receptor or progesterone receptor positive. Adjuvant endocrine therapy (AET), including tamoxifen or aromatase inhibitors (AI) such as letrozole, exemestane or anastrozole, is recommended for early stage hormone receptor positive patients. In post-menopausal women with early breast cancer, AI

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therapy is shown to be superior to tamoxifen in improving breast cancer mortality and reducing recurrence rates (Dowsett et al., 2010; Ryden et al., 2016). Non-adherence to medication is associated with increased mortality and higher risk of recurrence among breast cancer patients (Hershman et al., 2011; Hsieh et al., 2014; Makubate et al., 2013).

In a recent systematic review (Lin et al., 2017) on psychosocial factors for oral anticancer medication adherence among breast cancer patients, the most commonly reported facilitators of adherence were patient-provider relationships as well as positive views and beliefs of medication. In particular, the ability to discuss treatment options with the physician, frequency of physician communication and perception on the benefits of therapy were positively associated with adherence. Conversely, negative emotions such as annoyance or reluctance towards endocrine therapy as well as concerns about adverse effects of AI therapy, such as joint pains, weight gain and gynaecological symptoms, were associated with non-adherence. These psychosocial factors are among the items measured in the Beliefs about Medicines Questionnaire© (BMQ) (Horne et al., 1999) and the Adherence Starts with Knowledge (ASK-12) Questionnaire (Matza et al., 2009) (Appendix 1). The BMQ and ASK-12 questionnaires capture different aspects of medication behaviour and beliefs about medication which may affect adherence.

Cultural and sociodemographic differences in health behaviours and beliefs may also impact medication adherence. Horne et al. (2004) found that university students who were identified as having an Asian cultural background were more likely than those who were identified as European to have a negative perception towards medication in terms of harms and overuse. A study in Singapore showed that traditional medicine use was prevalent in cancer patients, and 37% of cancer patients believed that complementary and alternative medicine are at least as effective as conventional Western therapy in treating cancer (Chow et al., 2010). Asian patients also believed Western medicine to be 'toxic' but did not associate such toxicities with traditional herbal medicine (Kumar et al., 2016). In postmenopausal women with breast cancer who were on AET, sociodemographic characteristics such as age, being non-White, not married, and having lower income were associated with non-adherence although it was unclear whether other underlying factors (e.g. lack of trust in physicians, lack of comprehension of medication handling) were responsible in explaining these associations (Lin et al., 2017; Salgado et al., 2017). However, there is a dearth in information regarding psychosocial factors affecting medication adherence amongst breast cancer patients in the Asian region (Moon et al., 2017). Although the BMQ has been widely used to explore the relationship between beliefs associated with medication and adherence in various countries and disease settings (Foot et al., 2016; Horne et al., 2013), there has not been any such studies involving breast cancer patients in Asia. Our validation study is conducted in Singapore, which has a multi-ethnic population. The major ethnic groups have ancestral origins from various parts of Asia, including China, Malaysia and India.

The BMQ was originally developed for patients with the following conditions: asthma, diabetes, psychiatric disorders, cardiac and renal disease (Horne et al., 1999). It has since been validated in other medical conditions (Brett et al., 2017; Cinar et al., 2016; Topp et al., 2016; Wei et al., 2017). Beliefs influencing patients' evaluations of prescribed medicines can be categorised into two factors: Necessity (perceptions of personal need for treatment) and Concerns (of potential adverse effects of medications). In a meta-analytic review about the Necessity-Concerns Framework utilised in the BMQ (Horne et al., 2013), only 2 out of 94 studies involved breast cancer patients. Both studies were conducted in the UK, with one study in patients taking capecitabine (Bhattacharya et al., 2012) and another involving majority White patients in remission who were prescribed tamoxifen (Grunfeld et al., 2005). A more recent study evaluated the psychometric properties of the BMQ in predominantly white Caucasian women taking AET following early stage breast cancer (Brett et al., 2017). Furthermore, although

the ASK-12 questionnaire has been validated in patients with asthma, congestive heart failure and diabetes (Matza et al., 2009), validation studies have however not been conducted in cancer patients. As such, the objective of this study is to validate the BMQ and ASK-12 as measures of psychosocial factors of medication adherence in a Singapore population with early stage breast cancer.

## Methods

### Study design

Women on AET for early stage breast cancer were recruited from the National University Cancer Institute and Ng Teng Fong General Hospital in Singapore. Participants in this study ($n = 157$) were part of a randomised controlled trial to assess the effect of text message reminders on medication adherence (Tan et al., 2020). The trial protocol has been previously described (He et al., 2018). The eligibility criteria for the RCT were women aged at least 21 years with breast cancer, who had been prescribed AET for at least a year and would continue on AI therapy for at least another year. The study co-ordinator administered the BMQ and ASK-12 questionnaires via face-to-face interview during the baseline visit and 1-year follow up. Face-to-face interview, which was scheduled during the follow-up of the trial, was conducted to encourage participation and provide clarification. As suggested by Kühne (2018), being familiar with the same interviewer who administered the questionnaire, the participants would be more likely to answer truthfully and give less social desirability biased answers. For this validation study, we included interviews conducted in English, which was the preferred language of communication for all participants in this study. Only the baseline interviews were included lest the intervention might have affected participants' responses. We collected the following sociodemographic and clinical variables at baseline: age, ethnicity, education level, number of comorbidities, stage of breast cancer, duration of breast cancer diagnosis and duration of adjuvant endocrine therapy.

### Measures

For a more holistic view of facilitators and barriers, we administered the BMQ and ASK-12 questionnaires, briefly described below, to understand the attributes that influence medication adherence.

#### BMQ *(Horne et al., 1999)*

The BMQ is an 18-item questionnaire which consists of two components assessing patient's perceptions towards medications:

(i) BMQ-Specific
The two subscales of BMQ-Specific assess beliefs about a specific medication prescribed for an illness, corresponding to the themes Specific-Necessity (five items) and Specific-Concerns (five items). The former examines the beliefs of necessity towards taking a specific medication, in this case AET, while the latter examines concerns about the negative effects of medication.

(ii) BMQ-General
The two subscales of BMQ-General assess beliefs about medication in general, corresponding to the themes General-Overuse (four items) and General-Harm (four items). The first examines the beliefs of pharmaceutical management by doctors, while the latter examines the perceived harmful effect caused by the medicine.

The responses in all subscales are recorded on a five-point Likert scale (1 = Strongly disagree, 2 = Disagree, 3 = Uncertain, 4 = Agree, 5 = Strongly Agree). Higher scores indicate stronger beliefs in the concepts represented by the subscales.

#### ASK-12 *(Matza et al., 2009)*

The ASK-12 is a 12-item questionnaire measuring a patient's behaviour and barriers towards medication adherence. It consists of three subscales; two barrier subscales: Inconvenience/Forgetfulness (three items assessing the

reasons for non-adherence), Health Beliefs (four items assessing patients' beliefs about their medications, health goals and treating clinician), and one Behaviour subscale (five items asking patients to report how recently they have been non-adherent). The responses are recorded on a five-point Likert scale (Items 1–7: 1 = Strongly agree, 2 = Agree, 3 = Neutral, 4 = Disagree, 5 = Strongly disagree; items 8–12: 1 = In the last week, 2 = In the last month, 3 = In the last 3 months, 4 = More than 3 months ago, 5 = Never). Higher scores indicate greater barriers to adherence. Items in Inconvenience/Forgetfulness (items 1–3) and Behaviour (items 8–12) domains are scored in reverse.

### Statistical analysis

*Descriptive statistics.* The BMQ and ASK-12 domains were summarised in terms of range, skewness, percentage of ceiling, and floor effects. Ceiling or floor effects were considered to be present if more than 15% of participants responded with the highest or lowest possible score (Terwee et al., 2007). Skewness was considered to be substantial if it was beyond the range of −1 to +1 (Hair, 2006).

*Internal consistency.* The item-scale correlation (corrected for overlap) was evaluated, with the criterion for convergence being a correlation of more than 0.3 (Fayers and Machin, 2007). The internal consistency of the item scales was evaluated using the Cronbach's alpha ($\alpha$), where estimates greater than or equal to 0.7 were considered as reliable (Tavakol and Dennick, 2011).

*Factor analysis.* Structural validity was assessed via confirmatory factor analysis (CFA) using maximum likelihood estimation to establish consistency with the original constructs of the BMQ and ASK-12 questionnaires. The models were assessed on the basis of multiple fit indices, namely model chi-square, confirmatory factor index (CFI), root mean square error of approximation (RMSEA) and standardised root mean squared residual (SRMR). The following cut-offs were recommended (Acock, 2013): CFI $> 0.95$, RMSEA $< 0.08$ (reasonably close fit) or $< 0.05$ (good fit) and SRMR $< 0.08$. Standardised factor loadings greater than 0.50 were considered strong (Hair, 2006).

If the model fit and factor loadings were unsatisfactory, exploratory factor analysis (EFA) based on principal components analysis with varimax rotation were performed on the BMQ and ASK-12 items to assess the factor structure. It was suggested that it would be appropriate to proceed with EFA when the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy exceeded 0.50 and Bartlett's test of sphericity, an indicator of sufficient correlation among the variables showed $p < 0.05$ (Hair, 2006). As in the original study, the EFA was performed separately for the Barrier and Behaviour subscales in ASK-12 because of the difference in response options (Matza et al., 2009). Although a common rule of thumb was to retain only those components whose eigenvalues exceed one (Kaiser, 1960), a scree plot was also used as a guide to decide on the number of factors to be included. As Cattell had proposed, the first point on the 'straight' line and all points preceding it were retained in the subsequent analysis (Cattell, 1966).

All analyses were performed using STATA version 14, assuming a two-sided test at the 5% level of significance.

### Data sharing statement

De-identified individual participant response to questionnaires (including data dictionaries), statistical analysis code and output are available. Please note this dataset is available on FigShare.

## Results

The participants were enrolled from May 2015 to Dec 2018. Women diagnosed with breast cancer receiving AET were included in this study ($n = 157$). Their median age was 60.3 years (range 32–80). There were 67.5% Chinese, 14.7% Malay, 12.1% Indian and 5.7% of other

**Table 1.** Baseline characteristics of study participants.

| Characteristic | All patients ($n=157$) |
|---|---|
| Median age (range), years | 60.3 (32–80) |
| Ethnicity (%) | |
| Chinese | 106 (67.5) |
| Malay | 23 (14.7) |
| Indian | 19 (12.1) |
| Others | 9 (5.7) |
| Education level (%) | |
| Primary and below | 11 (7.0) |
| Secondary | 88 (56.1) |
| Pre-university | 31 (19.8) |
| University | 27 (17.2) |
| Number of comorbidities (%) | |
| 0 | 42 (26.8) |
| 1 | 28 (17.8) |
| 2 | 37 (23.6) |
| ⩾3 | 50 (31.9) |
| Stage (%)* | |
| 0 | 1 (0.6) |
| I | 61 (38.9) |
| II | 61 (38.9) |
| III | 30 (19.1) |
| Median duration of breast cancer diagnosis (IQR), years | 2.2 (1.7–3.0) |
| Median duration of adjuvant endocrine therapy (IQR), years | 1.5 (1.2–2.4) |

*Four patients (2.6%) who had Nx could not have stage number calculated.

ethnicity. Majority of the patients (93.0%) had at least secondary level education. The distribution of breast cancer staging among the participants was Stage 0 (0.6%), Stage I (38.9%), Stage II (38.9%) and Stage III (19.1%). The median duration of breast cancer diagnosis and AET were 2.2 (inter-quartile range (IQR) 1.7–3.0) years, and 1.5 (IQR 1.2–2.4) years respectively (Table 1).

## Validity and internal consistency

*BMQ.* No ceiling effect was observed for the BMQ scales. Floor effects ranged from 0% to 5.1%. The item-scale correlations for BMQ-Specific ranged from 0.40 to 0.58 whereas that for BMQ-General ranged from 0.25 to 0.55 (Table 2). The BMQ-Specific subscales had acceptable reliability (Specific-Necessity $\alpha=0.71$, Specific-Concerns $\alpha=0.72$). The BMQ-General subscales had lower reliability (General Overuse $\alpha=0.52$, General Harm $\alpha=0.61$). There was low correlation between the Specific-Concerns and Specific-Necessity subscales ($r=0.13$) but moderate correlation was noted between the General-Overuse and General-Harm subscales ($r=0.61$). Skewness ranged from −0.13 to 0.18, which was insubstantial.

*ASK-12.* The item-scale correlations ranged from 0.07 to 0.48. Although there was no ceiling effect, floor effect (63.7%) was observed and reliability was particularly low ($\alpha=0.31$) for the Behaviour subscale. It was also below the acceptable value for the Barrier subscales (Health beliefs $\alpha=0.59$, Inconvenience/Forgetfulness $\alpha=0.42$). There was low inter-scale correlation, ranging from 0.04 to 0.35. Skewness ranged from 0.15 to 0.16 for the Barrier subscale but was substantial in the Behaviour subscale (2.55).

## Confirmatory factor analysis

*BMQ-Specific.* The fit statistics for the two-factor model did not meet the acceptable cut-off criteria ($\chi^2=83.76$, df=34, $p<0.001$; CFI=0.842; RMSEA=0.097; SRMR=0.088). Four items had factor loadings below 0.50, namely Item 1 ('My health, at present, depends on my medicine'), Item 6 ('My medicine is a mystery to me'), Item 7 ('My health in the future will depend on my medicine') and Item 10 ('My medicine protects me from becoming worse') (Figure 1).

*BMQ-General.* The fit statistics ($\chi^2=23.74$, df=19, $p=0.206$; CFI=0.975; RMSEA=0.040; SRMR=0.051) for the two-factor model met the recommended cut-offs. However, factor loadings were strong for only three out of eight items in the scale, namely Item 1 ('Doctors use too many medicines'), Item 3 ('Most medicines

**Table 2.** Summary measures of BMQ and ASK-12 scales at baseline ($n = 157$).

| Scale | BMQ | | | | | | ASK-12 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Specific# | | General (original) | | General (new) | | Barrier# | | Behaviour (original) | Behaviour (new) | |
| | Necessity ($k = 5$) | Concerns ($k = 5$) | Overuse ($k = 4$) | Harm ($k = 4$) | Overuse ($k = 5$) | Harm/physician behaviour ($k = 3$) | Health beliefs ($k = 4$) | Inconvenience/ forgetfulness ($k = 3$) | Behaviour ($k = 5$) | Intentional non-adherence ($k = 3$) | Unintentional non-adherence ($k = 2$) |
| Item-scale correlation range* | 0.40–0.51 | 0.36–0.58 | 0.25–0.35 | 0.32–0.55 | 0.41–0.56 | 0.36–0.38 | 0.30–0.43 | 0.17–0.32 | 0.07–0.48 | 0.19–0.39 | – |
| $\alpha$ | 0.71 | 0.72 | 0.52 | 0.61 | 0.71 | 0.56 | 0.59 | 0.42 | 0.31 | 0.43 | – |
| Skewness | –0.10 | –0.13 | 0.02 | 0.18 | 0.20 | –0.11 | 0.15 | 0.16 | 2.55 | 3.25 | 2.17 |
| % Ceiling | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.64 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| % Floor | 0.64 | 5.10 | 0.0 | 1.91 | 0.64 | 1.91 | 3.18 | 11.46 | 63.69 | 82.80 | 75.80 |

k: number of items in the scale.
#BMQ-Specific and ASK-12 Barrier (health beliefs and inconvenience/forgetfulness) had the same items loaded onto the factors as the original factor structure.
*Correlation of each item with the rest of the items in the scale.

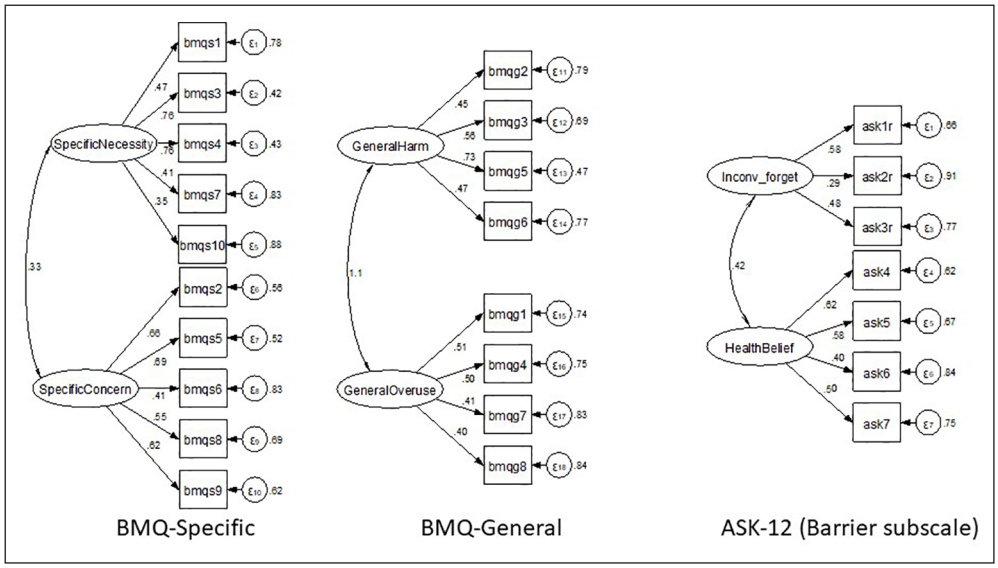


**Figure 1.** Confirmatory factor analysis model for BMQ-Specific, BMQ-General and ASK-12.

are addictive') and Item 5 ('Medicines do more harm than good') (Figure 1).

*ASK-12.* The two-factor model for Barrier subscale showed good fit ($\chi^2 = 12.51$, df = 13, $p = 0.486$, CFI = 1.00, RMSEA = 0.00 and SRMR = 0.044) but the one factor model for the Behaviour subscale could not converge. Factor loadings were weak for three out of seven items in the scale, namely Item 2 ('I run out of medicine because I don't get refills on time'), Item 3 ('Taking medicines more than once a day is inconvenient') and Item 6 ('I have someone I can call with questions about my medicines') (Figure 1).

## *Exploratory factor analysis*

As none of the scales performed well on both fit statistics and factor loadings, we performed EFA on all scales after checking that KMO and Bartlett's test of sphericity indicated that the data was suitable.

The KMO for all subscales exceeded 0.5 – BMQ-Specific (0.712), BMQ-General (0.814), ASK-12 Barrier (0.664) and ASK-12 Behaviour (0.528). Bartlett's test of sphericity was statistically significant for all subscales ($p < 0.001$).

*BMQ-Specific.* The scree plot (Supporting Information 1) and factor loadings (Supporting Information 2) suggested that a two-factor solution for BMQ-Specific was the most parsimonious. The factor structure corresponded with the original structure of BMQ-Specific. Factor 1 labelled as Specific-Concerns and Factor 2 Specific-Necessity, explained 48.9% of the total variance, with factor loadings ranging from 0.57 to 0.75 (Table 3).

*BMQ-General.* The scree plot (Supplemental Figure 2) and factor loadings (Supplemental Figure 3) suggested that a two-factor solution for BMQ-General was the most parsimonious. The factor structure of BMQ-General did not correspond with the original structure. Two items from the General-Overuse and three items from the General-Harm subscales loaded onto Factor 1 (renamed General-Overuse) and the remaining items onto Factor 2 (renamed General-Harm/Physician Behaviour (Table 3)). The factor structure explained 50.0% of the total variance, with factor loadings ranging from 0.60 to 0.74.

*ASK-12.* The scree plot (Supplemental Figure 2) and factor loadings (Supplemental Figure 3)

**Table 3.** Factor structure and loadings of the BMQ from exploratory factor analysis ($n = 157$).

| BMQ-Specific | Original component | Factor 1 (concerns) | Factor 2 (necessity) |
|---|---|---|---|
| S2. Having to take medicine worries me | SC | **0.7284** | 0.0421 |
| S5. I sometimes worry about long-term effects of my medicine | SC | **0.7509** | 0.0426 |
| S6. My medicine is a mystery to me | SC | **0.5741** | −0.1726 |
| S8. My medicine disrupts my life | SC | **0.6532** | 0.0187 |
| S9. I sometimes worry about becoming too dependent on my medicine | SC | **0.6731** | 0.1969 |
| S1. My health, at present, depends on my medicine | SN | −0.1706 | **0.7528** |
| S3. My life would be impossible without my medicine | SN | 0.3180 | **0.6689** |
| S4. Without my medicine I would be very ill | SN | 0.3138 | **0.6561** |
| S7. My health in the future will depend on my medicine | SN | 0.1069 | **0.6153** |
| S10. My medicine protects me from becoming worse | SN | −0.1553 | **0.6556** |
| Total variance explained (%) | | 25.68 | 23.26 |
| BMQ-General | | Factor 1 (overuse) | Factor 2 (harm/ physician behaviour) |
| G1. Doctors use too many medicines | GO | **0.5997** | 0.2468 |
| G2. People who take medicines should stop their treatment for a while every now and again | GH | **0.6658** | 0.0504 |
| G3. Most medicines are addictive | GH | **0.7389** | 0.0989 |
| G4. Natural remedies are safer than medicines | GO | **0.6425** | 0.1213 |
| G5. Medicines do more harm than good | GH | **0.6095** | 0.4688 |
| G6. All medicines are poisons | GH | 0.1371 | **0.7280** |
| G7. Doctors place too much trust on medicines | GO | 0.0936 | **0.7329** |
| G8. If doctors had more time with patients they would prescribe fewer medicines. | GO | 0.1602 | **0.6598** |
| Total variance explained (%) | | 27.33 | 22.63 |

The exploratory factor analysis was performed using principal components analysis with varimax rotation.
Factor loadings above 0.5 are shown in bold.
GH: general harm; GO: general overuse; SC: specific concerns; SN: specific necessity.

suggested that a two-factor solution was the most parsimonious for each of the Barrier and Behaviour subscales. The factor structure corresponded to the original Barrier subscale, with four items mapped to Factor 1 (Health Beliefs), and three items mapped to Factor 2 (Inconvenience/Forgetfulness) (Table 4). The factor structure explained 46.1% of the total variance, with factor loadings ranging from 0.51 to 0.77. For the Behaviour subscale, items 8, 9 and 10 loaded onto Factor 1 (renamed Intentional non-adherence) which captured non-adherent behaviours associated with not following prescription orders, perception of medication ineffectiveness and side effects. Items 11 and 12 loaded on Factor 2 (renamed Unintentional non-adherence) and comprised non-adherent behaviours related to cost, and unavailability of medicines at the time of administration. The factor structure explained 58.0% of the total variance, with factor loadings ranging from 0.54 to 0.83.

## *Analysis of new factor structure*

The new factor structures of BMQ-General and ASK-12 are presented in Table 2. The internal

**Table 4.** Factor structure and loadings of the ASK-12 from exploratory factor analysis ($n = 157$).

| Barrier subscale | Original component | Factor 1 (health beliefs) | Factor 2 (inconvenience/ forgetfulness) |
|---|---|---|---|
| 1. I just forget to take my medicines some of the time. | IF | 0.0677 | **0.7651** |
| 2. I run out of my medicine because I don't get refills on time. | IF | 0.1309 | **0.5127** |
| 3. Taking medicines more than once a day is inconvenient. | IF | 0.0547 | **0.7075** |
| 4. I feel confident that each one of my medicines will help me. | HB | **0.7013** | 0.1845 |
| 5. I know if I am reaching my health goals. | HB | **0.6918** | 0.1035 |
| 6. I have someone who I can call with questions about my medicines. | HB | **0.5573** | 0.1175 |
| 7. My doctor/nurse and I work together to make decisions. | HB | **0.7147** | −0.0680 |
| Total variance explained (%) | | 25.95 | 20.17 |
| Behaviour subscale | | Factor 1 (intentional nonadherence) | Factor 2 (unintentional nonadherence) |
| 8. Taken a medicine more or less often than prescribed? | BH | **0.8260** | −0.0626 |
| 9. Skipped or stopped taking a medicine because you didn't think it was working? | BH | **0.7191** | 0.4181 |
| 10. Skipped or stopped taking medicine because it made you feel bad? | BH | **0.5447** | −0.2497 |
| 11. Skipped, stopped, not refilled or taken less medicine because of the cost? | BH | −0.0102 | **0.7400** |
| 12. Not had medicine with you when it was time to take it? | BH | 0.0777 | **0.7813** |
| Total variance explained (%) | | 30.05 | 27.98 |

The exploratory factor analysis was performed using principal components analysis with varimax rotation.
Factor loadings above 0.5 are shown in bold.
BH: behaviour; HB: health belief; IF: inconvenience/forgetfulness.

consistency of BMQ-General ($\alpha = 0.52–0.61$) and ASK-12 Behaviour scale ($\alpha = 0.31$) improved with the new factor structure obtained from EFA (BMQ-General $\alpha = 0.56–0.71$; ASK-12 $\alpha = 0.43$).

## Discussion

Latent constructs such as health beliefs are not directly observable and are often measured via self-reported instruments. Although validation of the BMQ and ASK-12 has been performed in various populations and disease profiles, there could be differences due to sociocultural practices and disease-specific beliefs which affect medication adherence.

To our knowledge, this is the first study that validated the BMQ and ASK-12 among breast cancer patients on AET in Asia. For BMQ-Specific, our study showed similar internal consistency ($\alpha = 0.71–0.72$) with the original study ($\alpha = 0.55–0.86$) by Horne et al. (1999) and another study examining the psychometric properties of the BMQ-AET among mostly Caucasian breast cancer patients ($\alpha = 0.78–0.80$) (Brett et al., 2017). The factor structure in

our study was also comparable to these two studies. Even though our factor loadings were lower, all values were above 0.50, suggesting good reliability and structural validity of the BMQ-Specific. The item-scale correlations of between 0.36 and 0.58 were consistent with a study on hypertensive and diabetic patients in Malaysia (0.35–0.64) (Supramaniam et al., 2019; Tan et al., 2018), a country with shared sociocultural norms as Singapore due to its proximity and historical relations, albeit with different ethnic proportions. The internal consistency of 0.52–0.61 based on the original BMQ-General scale was within the range reported by Horne et al. (1999) (0.47–0.83). Although the two-factor structure has been replicated in various studies (Cinar et al., 2016; Jimenez et al., 2017), the item ('Natural remedies are safer than medicines') tended to load onto General Harm rather than General Overuse in these studies (Arikan et al., 2018; Komninis et al., 2013; Mahler et al., 2012). Some studies also reported a one-factor solution (De las Cuevas et al., 2011; Samalin et al., 2017; Supramaniam et al., 2019).

There was significant floor effects in the ASK-12 Behaviour subscale, which could be a possible reason for the non-convergence of the CFA model. Matza et al. (2009) reported floor effects of 50.9%–56.3% for items 9–11, whereas the floor effects in our study were more apparent, ranging from 93.6% to 99.4%. This phenomenon suggested low barriers to adherence in terms of compliance to prescribed instructions, perceived inefficacy of medication, adverse effects and medication costs. However, it could also be attributed to social desirability bias. Of the patients who reported missing at least 1 day of letrozole in the last 3 months, 77.8% indicated that they had never taken a medicine more or less often than prescribed (ASK-12 item 8). The phrasing of the question with the word 'prescribed' could infer that they were following their doctor's orders because doctors were deemed of higher social hierarchy in most Southeast Asian countries (Claramita et al., 2011), therefore their instructions should be respected. In addition, the floor effect could also be a reflection that cost was not a barrier to medication adherence in our study population. In particular, 74.5% enjoyed subsidised healthcare rates and 99.4% had never skipped or taken less medicine because of cost (ASK-12 item 11).

## *Study limitation*

The recruitment strategy of our RCT would have excluded participants who did not have a mobile phone and participants prescribed adjuvant endocrine therapy for less than a year, who were otherwise eligible for this validation study. The trial participants might have been more familiar with their medication as compared to other patients newly initiated on adjuvant endocrine therapy.

The study has some limitations such as the absence of test-retest reliability data. The recommended interval for test-retest reliability is 2 weeks (Salkind, 2010). In our study, the interval between the first and the second assessment was 1 year which was too far apart for more meaningful test-retest analysis. Moreover, our participants were part of a randomised clinical trial to evaluate the effect of an SMS reminder on medication adherence. Thus, changes in test scores might have been affected by either intervention or a real change in the measured construct during the time between the administration of the two tests.

Factor solutions deviating from the original factors may be observed in patients of different backgrounds or comorbid conditions. For example, Samalin et al. (2017) reported a one-factor solution for BMQ-General in French patients with mental disorders. Similarly, Supramaniam et al. (2019) fitted all BMQ-General items onto the same factor amongst Malaysian patients with Type II diabetes mellitus. However, our study had limited sample size to allow a robust sensitivity analysis of other clinical subgroups. In our study, participants might also have found it difficult to distinguish between the Harm and Overuse concepts and

this was demonstrated in the high inter-scale correlation ($r=0.61$). The use of the original BMQ items might not have captured additional beliefs specific to participants of an Asian descent. Thus, future studies should explore an adaptation of the BMQ-General and ASK-12 in the Singapore population and confirm the new factor structure generated in our study.

### *Clinical implication*

Our findings suggest that BMQ-Specific is a valid instrument for understanding the beliefs about medication specific to AET amongst breast cancer patients in Singapore. For assessing beliefs about medication in general or understanding behaviour associated with medication adherence, adaptations of the BMQ-General and ASK-12 respectively may be required.

## Conclusion

The BMQ-Specific was found to be a valid and reliable instrument for breast cancer patients on AET in Singapore. Further studies and external validation are needed to confirm the best factor structure for BMQ-General and ASK-12 in Singapore.

### List of abbreviations

AET: adjuvant endocrine therapy; AI: Aromatase inhibitors; ASK: adherence starts with knowledge; BMQ: beliefs about medicines questionnaire; CFA: confirmatory factor analysis; CFI: confirmatory factor index; EFA: exploratory factor analysis; KMO: Kaiser-Meyer-Olkin; RMSEA: root mean square error of approximation; SRMR: standardised root mean squared residual.

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### Author contributions

AW, CCT, PW, SCL and BCT participated in the design of the study and research protocol. AW, CCT, SHT, LEYA, SEL, WQC, JH and SCL significantly contributed to patient recruitment. EHT collected the data. EHT and BCT conducted the statistical analysis. All authors were involved in the writing, editing and approval of the final manuscript.

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

### Ethics approval and consent to participate

The study was approved by the National Healthcare Group Domain-Specific Review Board (reference number 2014/01316). All procedures performed were in accordance with the ethical standards of the institution.

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### Informed consent

Written informed consent was obtained from all individual participants included in the study.

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## Supplemental material

Supplemental material for this article is available online.

## References

Acock AC (2013) *Discovering Structural Equation Modeling Using Stata*. Texas: Stata Press.

Arikan H, Duman D, Kargin F, et al. (2018) Cross-cultural adaptation and validation of beliefs about medicines questionnaire on asthma and chronic obstructive pulmonary disease patients. *Turkish Thoracic Journal* 19(1): 36–40.

Bhattacharya D, Easthall C, Willoughby KA, et al. (2012) Capecitabine non-adherence: Exploration of magnitude, nature and contributing factors. *Journal of Oncology Pharmacy Practice* 18(3): 333–342.

Brett J, Hulbert-Williams NJ, Fenlon D, et al. (2017) Psychometric properties of the Beliefs about Medicine Questionnaire-adjuvant endocrine therapy (BMQ-AET) for women taking AETs following early-stage breast cancer. *Health Psychol Open* 4(2): 2055102917740469.

Cattell RB (1966) The scree test for the number of factors. *Multivariate Behavioral Research* 1(2): 245–276.

Chow WH, Chang P, Lee SC, et al. (2010) Complementary and alternative medicine among Singapore cancer patients. *Annals Academy of Medicine Singapore* 39(2): 129–135.

Cinar M, Cinar FI, Acikel C, et al. (2016) Reliability and validity of the Turkish translation of the beliefs about medicines questionnaire (BMQ-T) in patients with Behcet's disease. *Clinical and Experimental Rheumatology* 34(6 Suppl 102): S46–s51.

Claramita M, Utarini A, Soebono H, et al. (2011) Doctor-patient communication in a Southeast Asian setting: The conflict between ideal and reality. *Advances in Health Sciences Education: Theory and Practice* 16(1): 69–80.

De las Cuevas C, Rivero-Santana A, Perestelo-Perez L, et al. (2011) Adaptation and validation study of the Beliefs about Medicines Questionnaire in psychiatric outpatients in a community mental health setting. *Human Psychopharmacology: Clinical and Experimental* 26(2): 140–146.

Dowsett M, Cuzick J, Ingle J, et al. (2010) Meta-analysis of breast cancer outcomes in adjuvant trials of aromatase inhibitors versus tamoxifen. *Journal of Clinical Oncology* 28(3): 509–518.

Fayers PM and Machin D (2007) *Quality of Life: The Assessment, Analysis and Interpretation of Patient-Reported Outcomes*. Chichester, England; Hoboken, NJ: John Wiley & Sons.

Foot H, La Caze A, Gujral G, et al. (2016) The necessity-concerns framework predicts adherence to medication in multiple illness conditions: A meta-analysis. *Patient Education and Counseling* 99(5): 706–717.

Grunfeld EA, Hunter MS, Sikka P, et al. (2005) Adherence beliefs among breast cancer patients taking tamoxifen. *Patient Education and Counseling* 59(1): 97–102.

Hair JF (2006) *Multivariate Data Analysis*. Upper Saddle River, N.J: Pearson Prentice Hall.

He Y, Tan EH, Wong ALA, et al. (2018) Improving medication adherence with adjuvant aromatase inhibitor in women with breast cancer: Study protocol of a randomised controlled trial to evaluate the effect of short message service (SMS) reminder. *BMC Cancer* 18(1): 727.

Hershman DL, Shao T, Kushi LH, et al. (2011) Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. *Breast Cancer Research and Treatment* 126(2): 529–537.

Horne R, Chapman SC, Parham R, et al. (2013) Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: A meta-analytic review of the Necessity-Concerns Framework. *PLoS One* 8(12): e80633.

Horne R, Graupner L, Frost S, et al. (2004) Medicine in a multi-cultural society: The effect of cultural background on beliefs about medications. *Social Science & Medicine* 59(6): 1307–1313.

Horne R, Weinman J and Hankins M (1999) The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology & Health* 14(1): 1–24.

Hsieh KP, Chen LC, Cheung KL, et al. (2014) Interruption and non-adherence to long-term adjuvant hormone therapy is associated with adverse survival outcome of breast cancer women–an Asian population-based study. *PLoS One* 9(2): e87027.

Jimenez K, Vargas C, Garcia K, et al. (2017) Evaluating the validity and reliability of the beliefs about medicines questionnaire in low-income, spanish-speaking patients with diabetes in the United States. *The Diabetes Educator* 43(1): 114–124.

Kaiser HF (1960) The application of electronic computers to factor analysis. *Educational and Psychological Measurement* 20(1): 141–151.

Komninis I, Micheli K, Roumeliotaki T, et al. (2013) Adaptation and validation of the Beliefs about Medicines Questionnaire (BMQ) in primary care patients in Greece. *European Journal for Person Centered Healthcare* 1(1): 224–231.

Kühne S (2018) From strangers to acquaintances? Interviewer continuity and socially desirable responses in panel surveys. *Survey Research Methods* 12(2): 121–146.

Kumar K, Greenfield S, Raza K, et al. (2016) Understanding adherence-related beliefs about medicine amongst patients of South Asian origin with diabetes and cardiovascular disease patients: A qualitative synthesis. *BMC Endocrine Disorders* 16(1): 24–24.

Lin C, Clark R, Tu P, et al. (2017) Breast cancer oral anti-cancer medication adherence: A systematic review of psychosocial motivators and barriers. *Breast Cancer Research and Treatment* 165(2): 247–260.

Mahler C, Hermann K, Horne R, et al. (2012) Patients' beliefs about medicines in a primary care setting in Germany. *Journal of Evaluation in Clinical Practice* 18(2): 409–413.

Makubate B, Donnan PT, Dewar JA, et al. (2013) Cohort study of adherence to adjuvant endocrine therapy, breast cancer recurrence and mortality. *British Journal of Cancer* 108(7): 1515–1524.

Matza LS, Park J, Coyne KS, et al. (2009) Derivation and validation of the ASK-12 adherence barrier survey. *Annals of Pharmacotherapy* 43(10): 1621–1630.

Moon Z, Moss-Morris R, Hunter MS, et al. (2017) Barriers and facilitators of adjuvant hormone therapy adherence and persistence in women with breast cancer: A systematic review. *Patient Preference and Adherence* 11: 305–322.

National Registry of Diseases Office (2015) Singapore cancer registry. Reportno. Report Number|, Date. Place Published|: Institution|.

Pathy NB, Yip CH, Taib NA, et al. (2011) Breast cancer in a multi-ethnic Asian setting: Results from the Singapore-Malaysia hospital-based breast cancer registry. *The Breast* 20 Suppl 2: S75–S80.

Ryden L, Heibert Arnlind M, Vitols S, et al. (2016) Aromatase inhibitors alone or sequentially combined with tamoxifen in postmenopausal early breast cancer compared with tamoxifen or placebo - Meta-analyses on efficacy and adverse events based on randomized clinical trials. *The Breast* 26: 106–114.

Salgado TM, Davis EJ, Farris KB, et al. (2017) Identifying socio-demographic and clinical characteristics associated with medication beliefs about aromatase inhibitors among postmenopausal women with breast cancer. *Breast Cancer Research and Treatment* 163(2): 311–319.

Salkind NJ (2010) *Encyclopedia of Research Design. SAGE Research Methods*. Thousand Oaks, CA: SAGE Publications, Inc.

Samalin L, de Chazeron I, Belzeaux R, et al. (2017) Exploratory analysis of the French version of the beliefs about medicines questionnaire in patients with severe mental disorders: Factorial structure and reliability in specific populations of schizophrenic, bipolar and depressive patients. *PLoS One* 12(3): e0173267.

Supramaniam P, Aisyah A, Chong L, et al. (2019) Reliability and validity of Beliefs on Medicine Questionnaire (BMQ) in diabetes mellitus patients: Malay Translated Version. *International Journal of Scientific and Research Publications* 9(2): 66–73.

Tan CS, Hassali MA, Neoh CF, et al. (2018) Cultural adaptation and linguistic validation of the beliefs about medicines questionnaire in Malaysia. *Value in Health Regional Issues* 15: 161–168.

Tan EH, Wong ALA, Tan CC, et al. (2020) Improving medication adherence with adjuvant aromatase inhibitor in women with breast cancer: A randomised controlled trial to evaluate the effect of Short Message Service (SMS) reminder. *The Breast* 53: 77–84.

Tavakol M and Dennick R (2011) Making sense of Cronbach's alpha. *International Journal of Medical Education* 2: 53–55.

Terwee CB, Bot SD, de Boer MR, et al. (2007) Quality criteria were proposed for measurement properties of health status questionnaires. *Journal of Clinical Epidemiology* 60(1): 34–42.

Topp M, Vestbo J and Mortensen EL (2016) Psychometric properties of the COPD-specific beliefs about medicine questionnaire in an outpatient population: A rasch-analysis. *Chronic Obstructive Pulmonary Diseases* 3(4): 748–757.

Wei L, Champman S, Li X, et al. (2017) Beliefs about medicines and non-adherence in patients with stroke, diabetes mellitus and rheumatoid arthritis: A cross-sectional study in China. *BMJ Open* 7(10): e017293.

**Appendix 1.** BMQ scale items.

| | |
|---|---|
| Specific-Necessity | S1. My health, at present, depends on my medicine |
| | S3. My life would be impossible without my medicine |
| | S4. Without my medicine I would be very ill |
| | S7. My health in the future will depend on my medicine |
| | S10. My medicine protects me from becoming worse |
| Specific-Concern | S2. Having to take medicine worries me |
| | S5. I sometimes worry about long-term effects of my medicine |
| | S6. My medicine is a mystery to me |
| | S8. My medicine disrupts my life |
| | S9. I sometimes worry about becoming too dependent on my medicine |
| General-Overuse | G1. Doctors use too many medicines |
| | G4. Natural remedies are safer than medicines |
| | G7. Doctors place too much trust on medicines |
| | G8. If doctors had more time with patients they would prescribe fewer medicines |
| General-Harm | G2. People who take medicines should stop their treatment for a while every now and again |
| | G3. Most medicines are addictive |
| | G5. Medicines do more harm than good |
| | G6. All medicines are poisons |

ASK-12 scale items.

| | |
|---|---|
| Inconvenience/ forgetfulness | 1. I just forget to take my medicines some of the time. |
| | 2. I run out of my medicine because I don't get refills on time. |
| | 3. Taking medicines more than once a day is inconvenient. |
| Health beliefs | 4. I feel confident that each one of my medicines will help me. |
| | 5. I know if I am reaching my health goals. |
| | 6. I have someone who I can call with questions about my medicines. |
| | 7. My doctor/nurse and I work together to make decisions. |
| Behaviour | 8. Taken a medicine more or less often than prescribed? |
| | 9. Skipped or stopped taking a medicine because you didn't think it was working? |
| | 10. Skipped or stopped taking medicine because it made you feel bad? |
| | 11. Skipped, stopped, not refilled, or taken less medicine because of the cost? |
| | 12. Not had medicine with you when it was time to take it? |